

REMARKS**I. Status of the Claims**

Claims 71, 72 and 80-83 are pending. Claims 71, 72 and 80-83 are rejected. Claim 71 has been amended above without any change in scope or content.

Applicant respectfully requests reconsideration of the claims in view of the following remarks.

II. Withdrawn Rejections

Applicant appreciates the Examiner's withdrawal of the rejection under 35 U.S.C. § 112.

Applicant also appreciates the Examiner's acknowledgment that the pending claims are patentable over Harris (US 3,944,391).

Applicant further appreciates the Examiner's withdrawal of the double patenting rejections.

III. Claims 71-72 and 80-83 are Patentable over Levin in view of Rice

Claims 71-72 and 80-83 are rejected under § 103(a) over Levin (US 3,915,805) in view of Rice (US 4,236,893). Applicant respectfully traverses the rejection.

The combination of Levin and Rice fails to teach or suggest all the elements of claims 71-72 and 80-83. Levin is directed to an *in vitro* turbidity assay for detecting endotoxin. Endotoxin is detected by admixing lysate of plasma-free *Limulus amebocytes* with a sample and measuring an increase in turbidity within the fluid. See claim 1 of Levin. Nowhere does Levin expressly disclose the use of an endotoxin binding protein immobilized on a solid support. In fact, Levin does not teach or suggest use of a solid support to immobilize any protein.

The deficiencies of Levin are not cured by Rice. Rice discloses measurement of antibodies in a sample using an antigen coated piezoelectric oscillator. See Abstract of Rice. Nowhere does Rice teach or suggest a biosensor device comprising an endotoxin binding protein immobilized on a solid support. In contrast, claims 71-72 and 80-83 each recite a biosensor device comprising endotoxin binding protein immobilized on a solid support or use of such a

device. The failure of the combination of Levin and Rice to teach or suggest all the elements of claims 71-72 and 80-83 indicates no *prima facie* case of obviousness has been established.

In addition, there is no suggestion or motivation to combine Levin and Rice. The Examiner asserts that Rice provides the proper motivation because “Rice teaches that piezoelectric oscillator means of analysis is inexpensive and unsophisticated and the results obtained are “rapid, accurate and objective measurements.” This reasoning is insufficient to provide the motivation to modify Levin with Rice. Issues of cost or sophistication simply do not provide the proper motivation to import selected pieces of Rice into Levin. The proper test is whether there exists some specific motivation or suggestion in Levin to modify Levin with the method of Rice, i.e., some specific motivation or suggestion must exist to import the piezoelectric oscillator of Rice into Levin, which fails to disclose, teach or suggest the use of any solid support to immobilize a protein. Because no such proper motivation or suggestion has been provided, no *prima facie* case of obviousness has been established.

With respect to the variety of different antibody/antigen relationships in Rice, the Examiner asserts that Rice “states that not only antibodies but other binding reagents such as *Staphylococcus aureus* or other cells which have surface receptors for certain types of immunoglobins can be used.” The Examiner, however, misinterprets Rice. The so-called “other binding reagents” do not participate in any antibody/antigen coated piezoelectric oscillator relationship. Instead, these “other binding reagents” bind to the antibody once the antibody binds to the antigen coated on the piezoelectric oscillator. See Col. 11, lines 9-11. In view of the above, no proper suggestion to modify the teachings of Levin with Rice has been provided.

In addition, no reasonable expectation of success has been provided. The Examiner asserts that because Rice discloses how to conjugate antigen onto an oscillator, that “one of ordinary skill in the art would know how to conjugate the protein in the amebocytes of the horseshoe crab to the oscillator.” Such generalized assertions are insufficient in establishing a reasonable expectation of success. Instead, objective evidence must be provided that establishes at least some degree of predictability exists. No such objective evidence has been provided.

Applicant respectfully requests withdrawal of the rejection.

IV. Claims 71-72 and 80-83 are Patentable over Levin in view of Oliveira

Claims 71-72 and 80-83 are rejected under § 103(a) over Levin (US 3,915,805) in view of Oliveira (US 4,242,096). Applicant respectfully traverses the rejection.

The combination of Levin and Oliveira fails to teach or suggest all the elements of claims 71-72 and 80-83. As discussed above, the solution turbidity assay of Levin is insufficient in that it fails to teach or suggest any endotoxin binding protein immobilized on a solid support. In fact, Levin fails to disclose, teach or suggest the use of any solid support to immobilize a protein.

Oliveira fails to cure the deficiencies of Levin. Similar to Rice, Oliveira discloses a piezoelectric oscillator coated with antigen. See Abstract. Nowhere does Rice teach or suggest a biosensor device comprising an endotoxin binding protein immobilized on a solid support.

In contrast, claims 71-72 and 80-83 each recites a biosensor device comprising endotoxin binding protein immobilized on a solid support or use of such a device. The failure of the combination of Levin and Oliveira to teach or suggest all the elements of claims 71-72 and 80-83 indicates no *prima facie* case of obviousness has been established.

In addition, there is no suggestion or motivation to combine Levin and Oliveira. The Examiner asserts that “the association between protein from horseshoe crab and endotoxin is similar to antibody/antigen binding.” Even assuming the Examiner’s assertions are true for argument purposes, it is improper to import the teachings of Oliveira into Levin, because Levin fails to disclose, teach or suggest the use of a solid support to immobilize a protein. Accordingly, no suggestion or motivation exists to modify Levin in the manner asserted by the Examiner.

Also, no reasonable expectation of success has been provided. That is, the Examiner has provided no objective evidence that supports successful modification of the solution turbidity assay of Levin using the methods taught by Oliveira. Accordingly, no *prima facie* case of obviousness has been established.

Applicant respectfully requests withdrawal of the rejection.

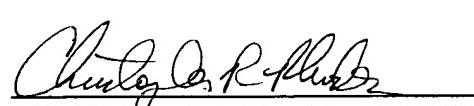
V. Conclusion

In view of the foregoing amendments and remarks, all claims in the application are in condition for allowance, and mailing of a Notice of Allowance is respectfully requested.

Respectfully submitted,
For Wainwright et al.

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Dated


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